

108. (New) The mammalian cell of claim 107 wherein said predetermined endogenous target gene is operatively associated with a nucleotide regulatory sequence heterologous to said predetermined endogenous target gene, so that expression of the target gene is controlled by said nucleotide regulatory sequence.

109. (New) The mammalian cell of claim 107 or 108 in which said mammalian cell does not grow readily in culture.

110. (New) The mammalian cell of claim 107 or 108 in which said mammalian cell is a human cell.

111. (New) The mammalian cell of claim 107 or 108 wherein said mammalian cell is a fibroblast, lymphocyte, epithelial cell or endothelial cell.

112. (New) The mammalian cell of claim 107 or 108 in which the predetermined endogenous target gene is a human gene.

113. (New) The mammalian cell of claim 107 or 108 in which the predetermined endogenous target gene encodes an interleukin, a growth factor, a colony stimulating factor, erythropoietin, a plasminogen activator, an enzyme, an interferon, or a receptor protein.

114. (New) The mammalian cell of claim 108 in which the predetermined endogenous target gene is normally not expressed by the mammalian cell.

115. (New) The mammalian cell of claim 107 or 108 in which the predetermined endogenous target gene is normally expressed by the mammalian cell.

116. (New) The mammalian cell of claim 108 in which the heterologous nucleotide regulatory sequence is a promoter, an enhancer or a promoter/enhancer.

117. (New) The mammalian cell of claim 108 in which the promoter/enhancer is a cytomegalovirus promoter/enhancer.

118. (New) The mammalian cell of claim 107 or 108 in which the amplifiable gene is dihydrofolate reductase, metallothionein-I, metallothionein-II, adenosine deaminase, or ornithine decarboxylase.

119. (New) The mammalian cell of claim 107 or 108 the genome of which further contains a selectable marker.

120. (New) The mammalian cell of claim 107 or 108 wherein said amplifiable gene is within 2 kb of said predetermined endogenous target gene.

121. (New) A human cell comprising an amplifiable gene at other than its wild-type site in the human genome and within the locus of a target gene expressing a protein to provide amplification of said target gene.

122. (New) A method for integrating an amplifiable gene into the genome of a mammalian cell that contains a predetermined endogenous target gene comprising inserting said amplifiable gene, by targeted homologous recombination, into the genome of said mammalian cell wherein said predetermined endogenous target gene is amplified when said amplifiable gene is amplified.

123. (New) The method of claim 122 which further comprises inserting with said amplifiable gene a nucleotide regulatory sequence heterologous to said predetermined endogenous target gene, by targeted homologous recombination, into the genome of said mammalian cell so that expression of said predetermined endogenous target gene is controlled by said nucleotide regulatory sequence.

124. (New) The method of claim 122 or 123 in which said mammalian cell does not grow readily in culture.

125. (New) The method of claim 122 or 123 in which said mammalian cell is a human cell.

126. (New) The method of claim 122 or 123 wherein said mammalian cell is a fibroblast, lymphocyte, epithelial cell or endothelial cell.

127. (New) The method of claim 122 or 123 in which the predetermined endogenous target gene is a human gene.

128. (New) The method of claim 122 or 123 in which the predetermined endogenous target gene encodes an interleukin, a growth factor, a colony stimulating factor, erythropoietin, a plasminogen activator, an enzyme, an interferon, or a receptor protein.

129. (New) The method of claim 123 in which the predetermined endogenous target gene is normally not expressed by the mammalian cell.

130. (New) The method of claim 122 or 123 in which the predetermined endogenous target gene is normally expressed by the mammalian cell.

131. (New) The method of claim 123 in which the heterologous nucleotide regulatory sequence is a promoter, an enhancer or a promoter/enhancer.

132. (New) The method of claim 123 in which the promoter/enhancer is a cytomegalovirus promoter/enhancer.

133. (New) The method of claim 122 or 123 in which the amplifiable gene is dihydrofolate reductase, metallothionein-I, metallothionein-II, adenosine deaminase, or ornithine decarboxylase.

134. (New) The method of claim 122 or 123 in which said genome further contains a selectable marker.

135. (New) The method of claim 122 or 123 wherein said amplifiable gene is within 2 kb of said predetermined endogenous target gene.

136. (New) A method for amplifying a predetermined endogenous target gene in the genome of a mammalian cell comprising:

(a) inserting an amplifiable gene, by targeted homologous recombination, into the genome of said mammalian cell wherein said predetermined endogenous target gene is amplified when said amplifiable gene is amplified;

(b) amplifying said predetermined endogenous target gene. --

REMARKS

Applicant has added new claims 107-136. Support in the specification for the new claims is as follows: